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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,220	10/06/1999	THOMAS HASLER	11002/002001	6146

7590

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EXAMINER

GRASER, JENNIFER E

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 07/17/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/355,220

Applicant(s)
Hasler et al.

Examiner
Jennifer Graser

Art Unit
1645



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Request for RCE & Amendt. C, 6/25/03
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-36 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) ☐ Other:

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DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/25/03 has been entered.

Claims 26-33 are currently pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 23 recites "a method for the isolation of polysaccharides"; however, the method in part (a) begins with 'a bacterial polysaccharide fraction', i.e., polysaccharides have already been isolated. It is suggested that the preamble be amended to recite "A method for the isolation of endotoxins from a polysaccharide fraction" because the

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current method would not adequately remove isolate polysaccharide from whole cell bacteria which is what the current preamble suggests.

Claim 23 is vague and confusing because of the new limitation “at which endotoxins are precipitated” because it is unclear what concentration this would encompass. The instant specification fails to recite “addition of alcohol to a final concentration *at which endotoxins are precipitated and* which is below the concentration at which the polysaccharide precipitates”. There is no support for this limitation. The passage Applicant refers to for support merely recites “addition of alcohol to a final concentration which is below the concentration at which the polysaccharide precipitates” and fails to mention anything about endotoxins precipitating prior to the depth filter stage. See also 112, first paragraph rejection below.

Claims 34 and 35 are vague and confusing because it is unclear whether the polymer filter is a deep bed filter. The specification indicates that the use of the depth bed filter is the novelty of the invention, yet claims 34 and 35 mention a polymer filter which is not necessarily a deep bed filter. Clarification is requested.

Claims 23-36 are vague and indefinite because it is unclear whether the deep bed filter is charged. The prior art seemed to indicate that a positively charged depth bed filter was required to trap endotoxins.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The new limitation “at which endotoxins are precipitated” in claim 23 appears to be new matter. The instant specification fails to recite “addition of alcohol to a final concentration *at which endotoxins are precipitated and* which is below the concentration at which the polysaccharide precipitates”. There is no support for this limitation. The passage Applicant refers to for support merely recites “addition of alcohol to a final concentration which is below the concentration at which the polysaccharide precipitates” and fails to mention anything about endotoxins precipitating prior to the depth filter stage. There is no teaching that the alcohol addition at step (b) precipitates endotoxins and there is no teaching of a concentration which would perform this function. Specific support must be identified by page and line number or the limitation must be removed from the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 23-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Gotschlich et al. or Schneerson et al (J.Exp. Med. 1980. 152:361-376) in view of Hou et al (J. Parenteral Science and Technology, 1990. 44(4): 204-209) and Lewis (US 5,589,591).

Gotschlich et al disclose a method of isolating polysaccharides from *N.meningitidis* which comprises using a detergent, Cetavlon, to rapidly precipitate polysaccharides from whole cell culture. Next ethanol is added to the solution and the mixture is centrifuged. The precipitate is then washed again with ethanol, then twice with acetone to remove the detergent and alcohol. See pages 1350-1351. Schneerson et al teach the isolation of polysaccharides from *H.influenzae* for use in immune compositions. The polysaccharides are isolated by using a detergent, Cetavlon, to rapidly precipitate polysaccharides from whole cell culture. Next ethanol is added to the solution and the mixture is centrifuged. The precipitate is then washed again with ethanol, then twice with acetone to remove the detergent and alcohol.

However, Schneerson and Gotschlich et al do not specifically teach the use of a polymer filter, deep bed filter, or depth filter, for the removal of endotoxins from the isolated polysaccharides.

Hou et al teach a method for removing endotoxins from bacterial polysaccharides using a depth filter or deep bed filter. Hou et al teach that the removal of these endotoxins is important for pharmaceutical purposes. Hou teaches that filtration methods using ultra filtration membranes or depth filters are popular means of depyrogenating biological solutions. The

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reference teaches that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes (see page 208). Lewis teaches that depth bed filters can be used to remove endotoxins.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a depth filter (deep bed filter) with a polymer filter to remove the endotoxins from the polysaccharides isolated by Gotschlich et al. or Schneerson because both Hou teaches that the endotoxins are highly toxic and must be removed from pharmaceutical products prior to use. Hou teaches that positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes (see page 208).

Changing the choice of filters is common in the art and often done to enhance yield and purification of a desired product. Further, the secondary reference, Hou et al., provides motivation in choosing a depth filter for removing endotoxin. Hou et al recite that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes (see page 208). Hou et al teach that the removal of these endotoxins from polysaccharides is very important for pharmaceutical purposes. Hou et al. teaches other methods of filtration, such as ultrafiltration, but this does not lead away from the choice of a deep bed filter because this passage is only in the Introduction portion of the reference where Hou recognizes that a more economical and convenient means for depyrogenating fluids in large volumes is needed. The basis of the article is to explore this new convenient and economical means, i.e., the use of the positively charged depth bed filter. The conclusion of the article, see

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page 208, states that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes. It appears that Hou et al. has identified a better alternative to the traditional filters known in the art. Further, the title of the Hou et al. reference is: "Depyrogenation by Endotoxin Removal with Positively Charged Depth Filter Cartridge". Lewis was merely cited to demonstrate that deep bed filters were commonly used in the art to remove endotoxins. Taken with the teachings of Hou, one of ordinary skill in the art would be clearly motivated to choose a positively charged depth bed filter. At the very least, these references have shown that the filters are obvious functional equivalents which can be interchanged depending on sample volume. It is noted that instant claims 34 and 35 do not require the use of a deep bed filter. Claim 35 recites "wherein the polymer filter and/or the deep bed filter is a polypropylene filter. The prior art clearly established that depth bed filters were more efficient than traditional filters for endotoxin removal from large volumes.

Additionally, the concentrations recited in dependent claims 30-32 are result effective variables. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of

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the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

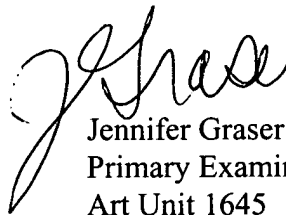
Since Applicant has not disclosed that the specific limitations recited in instant claims 30-32 are for any particular purpose or solve any stated problem and the prior art teaches that these concentrations often vary according to the specific sample being purified, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

 7/15/03
Jennifer Graser
Primary Examiner
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